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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,618	DUDLEY ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I, claims 1-41 (i.e. method of treating, preventing, or reducing the risk of developing a depressive disorder) and election of testosterone, isopropyl myristate, polyacrylic acid, ethanol, and methyltestosterone in the reply filed on 03/17/08 is acknowledged. Claim 42 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on 03/17/08.

Claims 1-42 are currently pending in the application. However, due to a restriction requirement, claim 42 is withdrawn from further consideration and claims 1-41 are being examined on the merits herein.

Thus the requirement is deemed proper and is therefore made final.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 120 for the earliest priority based on application 10/098,232, filed on 03/15/2002, which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or reducing the risk of developing a depressive disorder, **does not reasonably provide enablement for a method to prevent depressive disorder**. In fact, given that depressive disorder is caused by a combination of complex factors including neurotransmitter chemical imbalance and genetic factors, it would be impossible to prevent occurrence of depressive disorders since one has no control over genetic influences. Moreover, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Importantly, given that the term "prevention" implies an absolute term, it is assumed that no known disease or disease conditions can absolutely be prevented at this time. For example, applicant does not reasonably provide enablement for a method to prevent depressive disorder.

The instant claims are drawn to a method of preventing a depressive disorder, said method comprising administering a depressive-disorder effective amount of a

composition to an area of the skin of a subject for delivery of a steroid in the testosterone synthetic pathway to blood serum of the subject, wherein the composition comprises about 0.01-70% of the steroid in the testosterone synthetic pathway; 0.01-50% of a penetration enhancing agent; 0.01-50% of a thickening agent; and about 30-98% lower alcohol wherein the composition is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 µg per day of the steroid to the blood serum of the subject; and the percentages are on a weight basis of the composition.

Attention is directed to *In reWands,* 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method of preventing a depressive disorder, said method comprising administering a depressive-disorder effective amount of a

composition to an area of the skin of a subject for delivery of a steroid in the testosterone synthetic pathway to blood serum of the subject, wherein the composition comprises about 0.01-70% of the steroid in the testosterone synthetic pathway; 0.01-50% of a penetration enhancing agent; 0.01-50% of a thickening agent; and about 30-98% lower alcohol wherein the composition is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 µg per day of the steroid to the blood serum of the subject; and the percentages are on a weight basis of the composition. The nature of the invention is complex in that it encompasses preventing depressive disorder which is not probable. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites the fact that depressive disorders are caused by a combination of complex factors including neurotransmitter chemical imbalance and genetic factors, it would be impossible to prevent occurrence of depressive disorders since one has no control over genetic influences, and yet one cannot completely prevent depressive disorders and applicant does not provide sufficient support for preventing depressive disorder.

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term "prevention", the examiner will adopt the broadest reasonable interpretation for same. Webster's Ninth New Collegiate Dictionary defines "prevention" as "to keep from happening or existing", i.e., to completely eradicate.

The claims are thus very broad insofar as they recite the "prevention" of a depressive disorder, i.e., the complete eradication of same and "completely stop" of depressive disorder. While such "prevention" might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for preventing a depressive disorder. No reasonably specific guidance is provided concerning useful therapeutic protocols for preventing depressive disorder. The latter is not corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly composition could be predictably used to prevent depressive disorder as inferred by the aforementioned claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art

would have to engage in undue experimentation, with no assurance of success.

Genentech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

5. Suggested alternative language

Since the term "treating" is inclusive of various administrative timing schemes and thus provides adequate coverage for all reasonably successful therapies (prophylactic or active), the examiner recommends deleting the term "preventing".

The claims are examined herein for a method of treating or reducing the risk of developing a depressive disorder in a subject in need thereof, comprising administering a depressive-disorder effective amount of a composition to an area of the skin of a subject for delivery of a steroid in the testosterone synthetic pathway to blood serum of the subject, wherein the composition comprises about 0.01-70% of the steroid in the testosterone synthetic pathway; 0.01-50% of a penetration enhancing agent; 0.01-50% of a thickening agent; and about 30-98% lower alcohol wherein the composition is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 μg per day of the steroid to the blood serum of the subject; and the percentages are on a weight basis of the composition.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-28, and 30-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or reducing the risk of developing a depressive disorder using testosterone, does not reasonably provide enablement for a method of treating or reducing the risk of developing a depressive disorder using the **prodrug** or **derivative** of testosterone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. While applicant provides a definition for what a **prodrug** and a **derivative** of testosterone entail, applicant does not provide enablement for any **prodrug and/or derivative** of testosterone in the treatment of depressive disorder. Moreover, given that **a prodrug and/or a derivative** of testosterone may not necessarily be structurally similar; without delineating any working examples, the application fails to provide enablement for a method of treating depressive disorder using prodrug or derivatives of testosterone.

The instant claims are drawn to a method of treating, preventing, or reducing the risk of developing a depressive disorder using 1% testosterone, or a salt, ester, amide,

enantiomer, isomer, tautomer, prodrug, or derivative thereof. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention.

Attention is directed to *In reWands,* 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdApls1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method of treating, preventing, or reducing the risk of developing a depressive disorder using 1% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites the fact that derivatives and prodrugs are structurally different from testosterone and may not necessarily function like testosterone and applicant fails to provide enablement support.

2. The breadth of the claims

The claims are thus very broad insofar as they recite a method of treating, preventing, or reducing the risk of developing a depressive disorder using 1% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof yet applicant only provides enablement for treating depressive disorder using only testosterone.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for a method to treat depressive disorder using prodrugs or derivatives of testosterone. No reasonably specific guidance is provided concerning useful therapeutic protocols utilizing prodrugs or derivatives of testosterone in the treatment of depressive disorder.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to treat all functional bladder disorders as inferred by the claim and contemplated by the specification. Accordingly,

the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-11, 15-23, 25-38, and 41 are rejected under 35 U.S.C. 102 (e) as being anticipated by Dudley et al. (U.S. 6,503,894 B1).

Dudley et al. discloses that hypogonadism is linked to lowered mood and energy levels (i.e. depressive disorder; see col. 2, lines 32-36). Dudley et al. further teaches that as men age, there is a drop in testosterone levels which results in depressed mood (i.e. depressive disorder; see col. 3, lines 11-12, and 16-20 and col. 5, lines 15-17). Importantly, Dudley et al. teaches that treatment with a testosterone gel in a packet having a polyethylene liner administered daily via transdermal application results in increased positive mood (instant claims 1, 22-23, and 28-29; see col. 8, lines 1-11 and

fig. 23a-b, and col. 45, lines 1-17). The pharmaceutical gel composition of Dudley et al. may be administered percutaneously and may comprise at least one active pharmaceutical ingredient including testosterone and 17-methyltestosterone (i.e. elected species; instant claims 1, 29, and 41), one or more lower alcohols such as ethanol (i.e. elected species), a penetration enhancing agent such as isopropyl myristate, a thickener such as polyacrylic acid, particularly carbopol (a.k.a. carboxypolymethylene), water, salts, and stabilizers (instant claims 1-9 and 29-37; see col. 11, lines 54-57, and line 65, col. 12, lines 17-19, 49, and 60-61). Dudley et al. further exemplifies the composition in table 5, where a testosterone gel composition contained 1% testosterone, 0.90% carbopol 980 (i.e. thickener), 0.5% isopropyl myristate (i.e. penetration enhancing agent), 72.5% ethanol (i.e. lower alcohol) and 4.72% sodium hydroxide (instant claims 1-3, 6-7, 9-11, 29-32, 34-35, and 37-38; see col. 13, lines 25-43 and table 5). Dudley et al. demonstrated that application of the testosterone gel led to increased positive mood where patients received 5 g/day of testosterone gel led to 50 mg/day of testosterone being delivered to the skin or 10.0g/day which delivers 100 mg/day of testosterone (instant claims 18-19 and 21; see col. 14, lines 31, 34-35, and 46-49). While Dudley et al. does not explicitly teach what the skin delivering dose of a 7.5g/day of testosterone, Dudley inherently teach such dosage since a 7.5 mg dose will deliver at least 50 mg/day (based on the dose of 5g/day) and this reads on the limitation of claim 20 (instant claim 20). Dudley et al. further demonstrates that before administration, patients had a baseline of serum testosterone less than 300 ng/dL (instant claim 25) and that application of a 5.0g and a

10.0g testosterone gel results in 560ng/dL and 748ng/dL maximum serum testosterone respectively (instant claims 15-17) or where 0.1 g/day of the gel composition led to a 5ng/dL increase in serum testosterone concentration in just a few hours (see col. 18, lines 50-52, col. 19, lines 22-25 and table 8c, Cmax, col. 21, lines 26-29, and col. 23, lines 35-38). Finally, daily application up to 30 days of the 5.0 g testosterone gel resulted in serum testosterone of 490-570 ng/dL or application of 10.0g of testosterone gel resulted in 630-860 ng/dL (instant claims 26-28; col. 21, lines 25-30 and tables 5f-5h).

Accordingly, the teachings of Dudley et al. anticipate claims 1-11, 15-23,25-38 and 41.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-14 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Dudley et al. (U.S. 6,503,894 B1) as applied to claims 1-11, 15-23, 25-38, and 41.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The Dudley et al. reference is as described above and incorporated by reference herein. Dudley et al. does not particularly teach a composition weighing 1.0 grams to 10 grams, 2.5 grams to 7.5 g or a composition weighing about 5 grams.

However, it would have been well within the purview of a skilled artisan to vary the concentration of the ingredients of Dudley et al. if an increased or decreased effect is needed for a subject. Moreover, Dudley et al. teaches that the constituents may be varied (see col. 13, lines 36-43).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to vary the constituents of the composition of Dudley et al. since Dudley et al. teaches that the ingredients in his composition may be varied.

Moreover, it is generally noted that differences in concentration do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or percentages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.

Given that Dudley et al. teaches a percutaneous pharmaceutical gel composition for enhancing mood, one of ordinary skill would have been motivated to utilize the composition of Dudley et al. and vary the composition depending a subject's need with the reasonable expectation of providing a successful topical composition that is efficacious in increasing mood effect.

Claims 24 and 39-40 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Dudley et al. (U.S. 6,9503,894 B1) as applied to claims 1-23, and 25-38 and in view of Labrie et al. (U.S. 5,550,107).

The Dudley et al. reference is as described above and incorporated by reference herein. Dudley et al. does not particularly teach a composition provided as a separate component in a kit. Similarly, Dudley et al. does not teach the composition and the therapeutic agent in a kit or administered sequentially or simultaneously.

Labrie et al. teaches combination therapy administration involving anti-estrogens in combination with other hormones such as androgens (col. 1, lines 11-15 and col. 11, lines 32-33) which can be provided in a kit (instant claims 24 and 39; col. 5, lines 43-46), and either combined for a single pharmaceutical composition for simultaneous administration (see col. 6, lines 29-32) or provided as a multi-component kit (i.e. separate) for parenteral administration (see col. 25, lines 15-27 and col. 25-26, claims 8-14).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition of Dudley et al. in a kit for simultaneous administration since Labrie et al. teaches that combinatorial composition may be formulated in a kit and administered simultaneously. Given that Dudley et al. teaches a percutaneous pharmaceutical gel composition for enhancing mood, and Labrie et al. teaches that pharmaceutical composition for combination therapy can be provided in a kit for simultaneous administration, one of ordinary skill would have been motivated to formulate the composition of Dudley et al. in a kit with the reasonable expectation of

providing a successful topical composition that is easily handled and efficacious in increasing mood effect.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

05/05/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617